Case Reports

Inland Presentation of *Vibrio vulnificus* Primary Septicemia and Necrotizing Fasciitis

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Vibrio vulnificus, a halophilic *Vibrio* species recently described by Hollis and co-workers,[1] is part of the normal marine flora of Atlantic coastal and Gulf of Mexico waters.[2,3] This organism can be extremely virulent in humans and, as described by Blake and associates,[4] causes primarily two clinical syndromes in infected persons. Wound infections result from contact of wounds with saltwater harboring *V vulnificus* or from puncture wounds acquired by handling shellfish harvested from such environments. Primary septicemia is caused by ingesting raw shellfish (generally oysters) containing this *Vibrio* species and is characterized by the rapid development of sepsis, secondary metastatic skin lesions and a mortality rate as high as 67%.[4,5]

Cases of *V vulnificus* primary septicemia in the United States have been clustered about the Atlantic and the Gulf seaboards, paralleling the ecology described for this *Vibrio* species.[3,4] No documented cases of primary septicemia have been reported in western states to our knowledge. In this article we report a case of *V vulnificus* primary septicemia in Salt Lake City, Utah.

Report of a Case

The patient, a 78-year-old man, was admitted to the University of Utah Medical Center in late August of 1983 with confusion, hypotension, blistering skin lesions and leg weakness. He had been traveling alone by train from New York City to the West Coast when, one day before arriving in Salt Lake City, he began to experience malaise, fatigue and leg weakness. Other passengers pointed out to train authorities that he was acting confused and that blistering lesions were developing on his legs; he was subsequently transported to the University of Utah Medical Center.

The patient appeared to have sustained thermal or chemical burns when he was first evaluated in the emergency room. Because of the persistence of hypotension refractory to vigorous volume replacement, he was admitted to the medical intensive care unit for evaluation of possible sepsis. Despite the gravity of his clinical condition, the patient showed an unusual lack of concern. He had had no thermal or chemical injury, prior lesions, trauma or any other exposures to his lower extremities. He had no gastrointestinal complaints or other symptoms to suggest an alternative source of infection.

The patient's past medical history was significant for peptic ulcer disease requiring occasional antacid use, alcohol abuse and an episode of jaundice occurring during a period of excessive alcohol intake. The development of alcoholic cirrhosis was suspected but a liver biopsy had not been done and medical follow-up had been infrequent.

On admission the patient's blood pressure was 50/30 mm of mercury and rose to 90/50 mm of mercury with fluid resuscitation. His pulse was 115 per minute and his temperature was 35.7°C (96.3°F). On physical examination he had moderate bilateral wheezes, bibasilar rales and distant heart sounds without murmur and his abdomen was normal to palpation without evidence of ascites or hepatosplenomegaly. The only physical evidence of liver disease was several spider angiomas. The lower extremities were remarkable for cyanosis to the midcalves and focal areas of necrosis and blistering. There were large ecchymotic bullous lesions with surrounding erythema and induration scattered about the knees and medial thighs (Figure 1). Distal pulses were greatly diminished. A neurologic examination showed lower extremity weakness and hypoesthesia below the knees. The patient had no meningeal signs.

Admission laboratory studies elicited the following values: hematocrit, 37.8%; leukocyte count, 3,900 per μl with 30% segmented and 37% banded neutrophils, 7% metamyelocytes, 20% lymphocytes and 6% monocytes; platelet count, 107,000 per μl; prothrombin time, 16.7 seconds; blood urea nitrogen, 52, serum creatinine, 3.5, and glucose, 39 mg per dl; creatine phosphokinase, 3,058 IU per liter with 13% muscle-brain fraction; total bilirubin, 1.1 mg per dl; albumin, 2.6 grams per dl; alkaline phosphatase, 74, lactic dehydrogenase, 237, aspartate aminotransferase, 120, and alanine aminotransferase, 119 IU per liter. There was a pronounced metabolic acidosis with a total carbon dioxide content of 9 mEq per liter, a lactic acid level of 11.1 mEq per liter and blood-gas determinations made with the patient breathing room air showed a pH of 7.21, a partial arterial oxygen pressure of 71 torr and a partial carbon dioxide pressure of 28 torr. Sinus tachycardia was noted on an electrocardiogram and the chest radiograph showed bilateral pulmonary interstitial edema. Examination of a cerebrospinal fluid specimen showed no abnormalities.

The patient was treated immediately with dopamine hydrochloride to maintain an adequate blood pressure. A right heart catheterization showed a mixed venous oxygen partial pressure of 38 torr, a central venous pressure of 16 mm of mercury, a pulmonary capillary wedge pressure of 20 mm of mercury and a systemic vascular resistance of 4.2 Wood units. Specimens of blood, sputum, urine, cerebrospinal fluid and leg lesions were cultured. The patient was treated with intravenous administration of nafcillin sodium and tobra-

(Jenkins RD, Johnston JM: Inland presentation of *Vibrio vulnificus* primary septicemia and necrotizing fasciitis. West J Med 1986 Jan; 144:78-80)

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Submitted, revised, March 14, 1985.

Reprints are not available.

mycin initially; rifampin and piperacillin sodium were added to the regimen several hours later. He also was given steroids intravenously, naloxone hydrochloride, 50% glucose, sodium bicarbonate, thiamine hydrochloride and aminophylline. Fasciotomies were done of both lower extremities and showed deep necrotizing fasciitis; bilateral above-the-knee amputations were recommended but the patient refused further operations. The lower extremities became increasingly more cyanotic and necrotic as unrelenting septic shock developed and the patient died 24 hours after admission to hospital. His family denied permission for a postmortem examination.

Subsequent discussion with family members revealed that the patient had eaten raw oysters and clams repeatedly during his visit to New York City. The last time he ate them was thought to have been the evening of departure, three days before hospital admission. Family members were unable to recall the source of the raw oysters.

Gram's stains of fluid and surgical specimens from the patient's leg lesions showed many polymorphonuclear leukocytes and Gram-negative bacilli. Several cultures of blood, wound and tissue specimens yielded the same Gram-negative bacillus, *Vibrio vulnificus*. The organism grew on sheep blood and MacConkey agar plates. The isolate was characterized as oxidase-positive, fermented glucose and lactose but not sucrose, it had positive reactions to lysine decarboxylase and *o*-nitrophenyl-β-D-galactopyranoside and the Voges-Proskauer test was negative. It was sensitive to ampicillin, mezlocillin, piperacillin, ticarcillin, cephalothin, cefoxitin, cefotaxime, moxalactam, chloramphenicol and gentamicin and resistant to amikacin and tobramycin, by disc elution susceptibility testing (Autobac IDX, General Diagnostics).

Discussion

This patient exhibited many of the clinical features described for *V vulnificus*-induced primary septicemia. These patients typically present with fever (92% to 94%), chills (82% to 91%) and hypotension (25% to 33%), with a mortality approaching 100% when hypotension occurs at the outset.[4-6] The incubation period for this extremely virulent organism is short, with symptoms appearing an average of 16 hours after exposure. Studies of virulence characteristics have suggested that *V vulnificus* is the most invasive of the *Vibrio* species.[7] Characteristic erythematous or purpuric skin lesions on the trunk and extremities have been noted frequently (67% to 75%) and often progress to vesicles, bullae and finally necrotic ulcers.[4] Lesions of diffuse cellulitis, acute myositis and necrotizing fasciitis have been described. On histologic examination, necrotizing vasculitis and Gram-negative bacilli are observed in skin and muscle biopsy specimens of these lesions.[4,6,8-11] Other features less consistently observed in primary septicemia include nausea, vomiting, abdominal pain and diarrhea. A significant portion of patients with *Vibrio vulnificus* septicemia have had preexisting hepatic disease. Cases have occurred predominantly in men (78% to 90%) older than 40 years (95%) and have been clustered temporally in the summer months.[4-6]

While our patient was an elderly man with known raw shellfish ingestion preceding the onset of septicemia, he had no fever, chills or gastrointestinal symptoms. He did have typical purpuric, bullous and necrotic skin lesions, and the organism was both seen on Gram's stain and isolated in cultures of specimens obtained from these lesions. The development of hypoesthesia of the lower extremities, probably a result of small vessel thrombosis with cutaneous nerve destruction, and the easy separation of fascial planes by blunt dissection are characteristic of necrotizing fasciitis. The patient was known to have a history of heavy alcohol consumption and probable alcohol-induced liver disease, predisposing him to both *V vulnificus* primary septicemia and to necrotizing fasciitis. Surgical intervention is usually necessary for this syndrome; however, our patient refused potentially life-saving amputations.

This case is important in several respects. The patient's illness was initially misdiagnosed as being caused by thermal or chemical injury because of the similarity of the lesions on the lower extremities to those seen with these more common injuries. It is the first documented case to our knowledge of *V vulnificus*-induced primary septicemia presenting in a western or inland state and, as such, does not conform to the established epidemiology of this disease. While documented clinical cases of *V vulnificus* primary septicemia have occurred in Belgium, Japan and Australia, most have been reported in states bordering the Gulf coast and Atlantic seaboard from Florida to New England.[5,6] Clinical isolates have been obtained from western (Hawaii, California) and inland (Pennsylvania, Arkansas and Wisconsin) states, but no case details have been reported.[1] Additionally, two inland cases of wound infection were recently traced to a New Mexico creek and an Oklahoma reservoir; *V vulnificus* was not recovered from either environmental source.[12] The organism has been identified from Atlantic and Gulf coastal waters[2,3] and from waters along the Pacific coast of Oregon.[13]

With the rapid mobility of today's society, persons can ingest raw shellfish from restaurants in states on the eastern

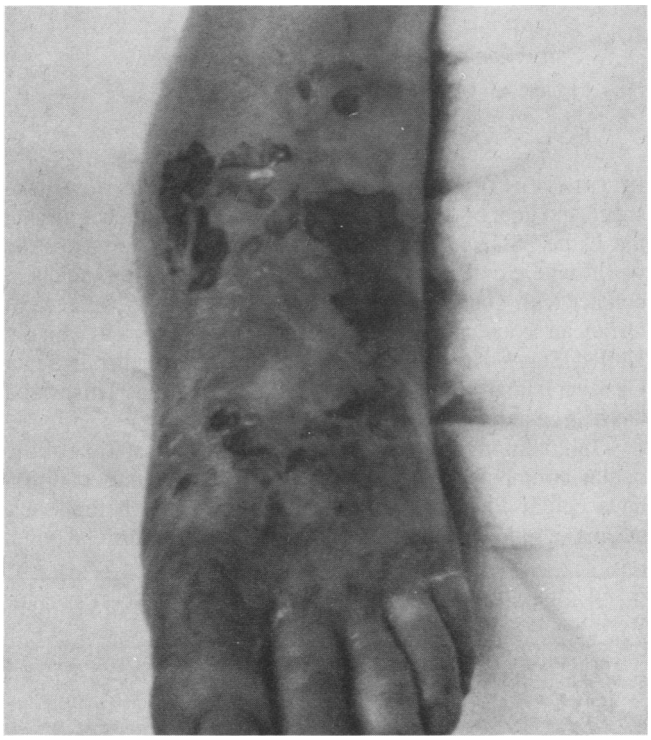

Figure 1.—Lower extremity skin lesions in a man with *Vibrio vulnificus* septicemia.

seaboard and be virtually anywhere in the United States by the onset of *V vulnificus* primary septicemia. Furthermore, raw oysters are often transported to distant inland restaurants and oyster bars where they can still harbor infectious organisms, even when transported under proper refrigeration. Although multiplication of *V vulnificus* is inhibited by storage at 4°C (39.2°F),[14] the organism has been recovered from oysters after four days of refrigeration.[15] Finally, although no documented cases of *V vulnificus* infections have been reported in patients in Pacific coastal states, the potential for acquiring both wound infections and septicemia in this part of the country exists.

Physicians caring for patients who present with signs and symptoms of necrotizing fasciitis should consider not only *Pseudomonas aeruginosa,* streptococci, staphylococci, anaerobes and facultative Gram-negative bacilli, but also halophilic *Vibrio* species, particularly *V vulnificus,* in the differential diagnosis. While the development of necrotizing fasciitis is usually related to local trauma or infection, it is uncommon as a manifestation of sepsis.[16] *V vulnificus* seems to be unique as a cause of necrotizing fasciitis from primary septicemia.[9,16] It may be prudent for western physicians to advise their patients who have hepatic disease or are otherwise immunocompromised to avoid eating raw seafood, particularly oysters, which filter and concentrate marine organisms.[5,17]

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Ophthalmomyiasis Externa in California

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INFESTATION OF HUMANS by the larvae of *Oestrus ovis,* the sheep and goat botfly, is a rare cause of acute conjunctivitis in the United States. It is not uncommon in other areas of the world where extensive sheep herding has brought humans in contact with goats and sheep. These areas include the Mediterranean countries, Central America and Africa.[1] In the United States, most cases have been reported from Santa Catalina Island, off the southern California coast. This island has a large indigenous wild goat population.[2-5]

Ophthalmomyiasis externa is the larval infestation of the ocular conjunctiva and adnexa. Patients with this condition have ocular foreign body sensation, redness, photophobia, tearing, a mild follicular conjunctivitis and a superficial punctate keratopathy.[4] Ophthalmomyiasis interna is intraocular larval penetration, primarily involving the choroid and retina. This can result in iridocyclitis, retinal detachment and endophthalmitis.[6,7] We recently examined and treated a patient with a severe external infestation of *O ovis* larvae.

(Heyde RRS, Seiff SR, Mucia J: Ophthalmomyiasis externa in California. West J Med 1986 Jan; 144:80-81)

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Submitted, revised, March 20, 1985.

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Report of a Case

The patient, a 28-year-old man, presented to the UCLA Medical Center emergency room complaining of 12 hours of bilateral ocular foreign body sensation, redness, pain and tearing. He reported that he had spent the day on Santa Catalina Island sightseeing and snorkeling in nearby kelp beds. After a dive, he surfaced and removed his goggles. He immediately noted stinging of both eyes, the right more than the left. Over the next four hours, his intermittent symptoms increased and became constant.

On examination in the emergency room, his visual acuity was 20/25, right eye, and 20/20, left eye. Pupils, ocular motility and visual fields were within normal limits. On external examination he had moderate edema of all four eyelids. Slit-lamp examination showed a mild conjunctival follicular reaction (Figure 1). A large number of small, translucent, white, motile larval organisms was noted in the upper and lower conjunctival fornices of both eyes (Figure 2). Occasionally they were seen traversing the bulbar conjunctiva and cornea. The right eye contained about 50 organisms with about 30 in the left. Both corneas showed superficial punctate staining.

A diagnosis of ophthalmomyiasis externa was made and 0.5% proparacaine hydrochloride and 4% cocaine hydrochloride were administered in an effort to decrease the motility of the organisms to aid in their removal. Copious irrigation resulted in reducing the infestation. Several organ-